PATENT
Attorney Docket No. **UM-03662**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Marc Peters-Golden *et al.*
Serial No.: 09/291,656 Group No.: 1653
Filed: 03/03/99 Examiner: K. Carlson
Entitled: **ADMINISTRATION OF PRODUCTS OF THE 5-LIPOXYGENASE METABOLIC PATHWAY TO ENHANCE ANTIMICROBIAL DEFENSE**

Transmittal of Appeal Brief

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: December 3, 2004 By: Traci E. Light

Sir or Madam:

Enclosed herewith please find Appellants Amended Brief, in response to the Notice of Non-Compliance to 37 CFR 1.192(c), mailed November 18, 2004. Applicants submitted a check in the amount of $165.00 to cover the cost of filing said brief, as required under § 1.17(c), on November 18, 2004.

The Commissioner is hereby authorized to charge payment of any fees associated with this communication or credit any overpayment to Deposit Account No. **08-1290. An originally executed duplicate of this transmittal is enclosed for this purpose.**

Dated: December 3, 2004

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This Brief contains these items under the following headings and in the order set forth below [37 CFR § 1.192(c)]:

I. REAL PARTY IN INTEREST

The real party in interest is the Regents of the University Of Michigan, 3003 South State Street, Ann Arbor, MI 48109-1280.

II. RELATED APPEALS AND INTERFERENCES

There are no related applications pending appeal.

III. STATUS OF CLAIMS

The present application (09/291,656), as filed on 03/03/99, originally contained Claims 1-26 as a divisional of the parent application (08/757,136; filed on 12/03/96) but Claims 1-21 were cancelled by way of a Preliminary Amendement leaving Claims 22-26 for examination. A First Non-Final Office Action (mailed 07/28/00) resulted in a response amending Claim 22 and the addition of new Claims 27-32 (mailed 01/03/01). A Notice Of Allowance was mailed 03/23/01. The Applicants then filed the Issue Fee and Formal Drawings (mailed on 06/25/01). A Second Non-Final Office Action (mailed 08/10/01) vacating the Notice Of Allowance with a new rejection resulted in a response amending Claims 22 and 28 and the addition of new Claims 33-37 (mailed 01/15/02). A First Final Office Action (mailed 05/07/02) resulted in a response (filed as a First RCE) amending Claims 22, 28, and 33 (mailed 09/09/02). A Third Non-Final Office Action (mailed 11/27/02) resulted in a response amending Claims 22, 28, and 33 (mailed 04/28/03). A Second Final Office Action (mailed 07/15/03) resulted in a response (filed as a Second RCE) amending Claims 22, 28, and 33 and canceling Claim 26 (mailed 01/15/04). A Third Final Office Action (mailed 03/24/04)

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rejected Claims 22-25 and 27-37, resulting in filing a Notice Of Appeal (mailed 08/23/04) to appeal Claims 22-25 and 27-37.

These appealed claims, as they now stand, are set forth in Appendix A (attached at Tab 1).

IV. STATUS OF AMENDMENTS

All amendments in the case have been entered.

V. SUMMARY OF THE INVENTION

Leukotrienes are potent mediators of inflammation derived from the 5-lipoxygenase pathway of arachidonic acid metabolism. The present invention contemplates the use of leukotrienes and other products of the 5-lipoxygenase pathway as an adjunct in the treatment of pneumonia and other lower respiratory tract infections.

The present inventors have determined that endogenous leukotrienes play an integral role in the host response to pulmonary infection. Even more importantly from a therapeutic standpoint, the present inventors found that exogenous leukotrienes exert pharmacologic actions which augment this response.

In one embodiment, the present invention contemplates an aerosol solution for the treatment of a microbial infection, the solution comprising a sterile liquid vehicle, an antibiotic and a leukotriene dissolved in the sterile liquid vehicle (Claim 22) where the infection might be caused by *Klebsiella pneumonia* (Claim 27, Claim 32, and Claim 37). In other embodiments, the above solution is in an intratracheal instillation device (Claim 28), or a nebulizer (Claim 33). In particular embodiments, the leukotriene is leukotriene B_4 (Claim

23, Claim 29, and Claim 34). In still further embodiments, the leukotriene is a cysteinyl leukotriene (Claim 24, Claim 30, and Claim 35); when the leukotriene is a cysteinyl leukotriene, it is leukotriene C_4, leukotriene D_4, or leukotriene E_4 in particular embodiments (Claim 25, Claim 31, and Claim 36).

VI. ISSUES

There are three issues on appeal:

A. Whether the Examiner used Gosselin *et al.* as proper prior art because Gosselin *et al.* was filed after Applicants' filing date and the parent application (602,059) does not disclose the claimed elements when rejecting Claims 22-25 and 27-37.

B. Whether the Examiner can avoid giving patentable weight to physical composition elements (*i.e.*, an aerosol) as interpreted by *Union Oil v. Atlantic Richfield; In re Rosicky; In re Riden et al., and In re Lerner* when rejecting Claims 22-25 and 27-37.

C. Whether the Examiner has made a proper *Prima Facie* case of obviousness when rejecting Claims 22-25 and 27-37.

VII. GROUPING OF CLAIMS

Each claim stands alone. Each claim has distinct limitations and must be considered independently.

Independent Claim 22 specifies a solution for the treatment of a microbial infection comprising an antibiotic and a leukotriene dissolved in a sterile liquid vehicle, wherein the solution is an aerosol. For example, this claim is not limited by the nature of the microbial infection or the types of antibiotic or leukotriene. The solution, however, is required to be an aerosol. Dependent Claims 23, 24, and 25, respectively, further specify that the leukotriene may be leukotriene B_4, a cysteinyl leukotriene, or selected from the group consisting of leukotriene C_4, leukotriene D_4, and leukotriene E_4. Dependent Claim 25, further specifies that at least one cause of the microbial infection results from a *Klebsellia pneumonia* infection.

Independent Claim 28 specifies a solution for the treatment of a microbial infection comprising an antibiotic and a leukotriene dissolved in a sterile liquid vehicle, wherein the solution is in an intratracheal instillation device, wherein this device is selected from the group consisting of an endotracheal tube and a bronchoscope. For example, this claim is not limited by the nature of the microbial infection or the types of antibiotic or leukotriene. The solution, however, is required to be contained within an intratracheal instillation device. Dependent Claims 29, 30, and 31, respectively, further specify that the leukotriene may be leukotriene B_4, a cysteinyl leukotriene, or selected from the group consisting of leukotriene C_4, leukotriene D_4, and leukotriene E_4. Dependent Claim 32, further specifies that at least one cause of the microbial infection results from a *Klebsellia pneumonia* infection.

Independent Claim 33 specifies a solution for the treatment of a microbial infection comprising an antibiotic and a leukotriene dissolved in a sterile liquid vehicle, wherein the solution is contained within a nebulizer. For example, this claim is not limited by the nature of the microbial infection or the types of antibiotic or leukotriene. The solution, however, is required to be contained within a nebulizer. Dependent Claims 34, 35, and 36, respectively, further specify that the leukotriene may be leukotriene B_4, a cysteinyl leukotriene, or selected from the group consisting of leukotriene C_4, leukotriene D_4, and leukotriene E_4. Dependent Claim 37, further specifies that at least one cause of the microbial infection results from a *Klebsellia pneumonia* infection.

VIII. ARGUMENT

A. Gosselin *et al.* Is Not Prior Art

United States Patent No.: 5,789,441 To Gosselin *et al.* (the '441 patent), as cited by the Examiner, was filed on February 11, 1997 as a continuation-in-part of the now abandoned United States Patent Application No. 08/602,059 To Gosselin *et al.* filed 02/15/96 (the '059 application)[1]. The Applicants' pending divisional application has priority to United States Patent Application No. 08/757,136, filed on December 3, 1996. Clearly, the '441 patent was filed after the Applicants' '136 application. As such, the Examiner must find complete support for the present rejection in the '059 parent application.

The Examiner has not (apparently) reviewed the '059 application for support regarding the present rejection. The '059 application does not teach any aerosol or sterile solution compositions. Consequently, the '441 patent's "aerosol" (Col. 11, line 31) and "sterile

[1] Applicants provided a copy of the '059 application to the Examiner in the *Second Final Office Action* response.

solution" (Col. 12, line 15) teachings do not enjoy the '059 application's priority date. Without support in the '059 application for the Applicants' claimed elements of "aerosols" and "sterile solutions" the '441 patent, therefore, is not prior art regarding the Examiner's present rejection.

B. An Aerosol Has Patentable Weight

The Examiner invokes legal case citations of *Union Oil, In re Rosicky, In re Riden et al.* and *In re Lerner* to support the proposition that "While the claims recite that the solution [is] aerosolized this phrase[ ] is given no patentable weight". *Third Final Office Action, pg. 3.*[2] The Applicants disagree. The Applicants' claimed embodiment is directed to a composition of matter comprising "an aerosol" and contains no functional language. Because "an aerosol" is not functional language the Examiner MUST give this claim element full patentable weight.

The Examiner cites *Union Oil Co. of California v. Atlantic Richfield Co., 208 F.3d 989, 54 USPQ.2D 227 (2000).* Applicants submit the issues in *Union Oil* involve very different claim language. The claims at issue in *Union Oil* describe a composition that is "suitable for" a particular use (*i.e.*, conventional gasoline to be used in a standard automobile engine). The CCPA upheld the lower court interpretation that the term "suitable for" encompassed any standard automotive fuel and was not directed to specialty fuels (*i.e.*, aviation or racing fuels).

The term "suitable for," however, does not appear in the present claims. Indeed, there is no attempt to create patentable limitations through "intended use" language such as "suitable

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[2] The Applicants note the Examiner no longer includes "intratracheal instillation devices" as lacking patentable weight in reference to this case law. In the Examiner's Answer, the Applicants request a clarification stating that a rejection to these novel features have been withdrawn.

for". Applicants' claims specify elements - not how the elements are used. For example, certain claims require that the solution is in the form of "an aerosol." This is not "suitable for" language - the term "aerosol" properly limits the form of the solution.

Second, the Examiner cites *In re Rosicky, 47 CCPA 859, 125 USPQ 341 (1960).* The Examiner is apparently relying on the *Rosicky* Court's rendering of a "pharmaceutical carrier" as obvious. This decision, however, was made in the context of the **absence** of any advantages established on-the-record:

> Appellant has not established by any sort of clinical data that such a quantity would be a safe or useful dosage for the treatment of any particular malady, or useful for the alleviation of specific symptoms.

In re Rosicky at 865. By contrast, several advantages of the proposed compositions are taught within the Applicants' specification and appear in boldface type below:

> A preferred mode of administration comprises administration to the lung. Patients who are sick enough to require **mechanical ventilation** can receive treatment with pharmacologic agents administered via the endotracheal tube which is connected to the ventilator. Alternatively, **intrapulmonary delivery** of pharmacologic agents to patients not requiring mechanical ventilation can be accomplished via aerosolization. Alternatively, the agent may be administered to the lung through a bronchoscope. Of course, the therapeutic agents may be investigated for their efficacy via other routes of administration, including parenteral administration. However, when the site of infection is the lung, **targeting drug delivery thereto is likely to minimize side effects and systemic consequences.**

Applicants' Specification, pg 22, ln 12 - 21 [emphasis added];

and,

> To ensure **dosing limited** to the respiratory tract and to be able to **precisely quantitate** the dose administered ... *Applicants' Specification, pg 53, ln 3 - 5.*
>
> [emphasis added]

Thus, contrary to the facts of *In re Rosicky,* Applicants' specification provides the requisite evidence showing particular advantages of an aerosol. As such, the holding of *In re Rosicky* has no bearing on the present claims.

The Examiner also cites *In re Lerner, 169 USPQ 51 (1971).* Applicants submit that *Lerner* is similar to *Rosicky* and is likewise inapplicable to the present claims. Specifically,

the *Lerner* decision notes that the limitation of a "carrier" in claim 4 of the particular application in question did not create a distinction over the art. However, a "carrier" is not analogous to limitations of the pending claims. A "carrier" is inert and frequently serves as nothing more than filler. By contrast, as noted above, an aerosol confers specific advantages as embodied in the presently claimed invention.

Finally, the Examiner cites *In re Riden et al., 138 USPQ 112 (1963).* Applicants remind the Examiner that a court holding may not be asserted without a determination as to whether the holding is still valid. Applicants point out that the rationale and holding of *In re Riden et al.*, relative to an obviousness rejection based on a primary reference that does not disclose or suggest any usefulness of a claimed composition, has been overruled:

> The question remains whether ... Riden state[s] the correct burden of proof to be imposed on an applicant for patent ... We have concluded that [it] does not. ... To the extent that ... Riden [is] inconsistent with the views expressed herein, they no longer will be followed, and are overruled. *In re Stemniski, 58 CCPA 1410; 444 F2d 581, 170 USPQ 343 (1971).*

Applicants argue, as detailed above, that the instant specification provides an ample showing of the advantages and usefulness for a composition comprising an aerosol. As held in *In re Stemniski*, it is not the Applicants' burden to prove a claim's non-obviousness to the Patent Office.

Thus, none of the four cases cited by the Examiner are applicable - let alone dispositive. None of the cases provides a basis or justification for ignoring the claim limitations at issue here.

C. Claims 22-25 and 27-37 Are Not *Prima Facie* Obvious

Even if the Examiner does not accept (improperly) that Gosselin *et al.* is not prior art, the Applicants submit that the Examiner still has not properly established the *prima facie* obviousness of the rejected claims. For example, the Examiner makes the conclusory statements:

> Therefore it would have been obvious to a person having ordinary skill in the art to include an antibiotic in a solution comprising a sterile liquid and a leukotriene ..., wherein the leukotrienes is LTB4 ..., or wherein the leukotrienes is a cysteinyl leukotriene ... such as leukotrienes C4, D4 and E4 ... because Gosselin et al. suggests to use LTB4 with an antibacterial or antifungal agent

> against Gram+ and - infections, or fungal infections. *Third Final Office Action* 03/24/04 pg. 3.

The Applicants disagree because the Examiner's statements are: i) unsupported and improper; ii) bald conclusions without a factual basis; and iii) Gosselin *et al.* does not teach all the claim limitations.

The Examiner admits that Gosselin *et al.* does not teach a leukotriene/antibiotic combination:

> Gosselin et al. do not expressly teach that to include an antibiotic to the [ ] solution comprising a sterile liquid and a leukotriene.

Third Final Office Action, 03/24/04 pg 3. Nevertheless, the Examiner maintains that Gosselin *et al.* is a proper 35 U.S.C. § 103(a) reference. The Applicants disagree.

For a proper rejection, each and every element within the claimed embodiment must be found in the cited art. *In re Vaeck*, 947 F.2d 488, 20 USPQ.2d 1438 (Fed. Cir. 1991); and *MPEP* § 2142; Establishing A *Prima Facie* Case Of Obviousness. The Applicants submit that Gosselin *et al.* lacks many of the claimed elements (*i.e.*, for example, aerosols, sterile liquid solutions, intratracheal instillation devices, and nebulizers). First, as noted above, the '441 patent disclosures of "a sterile liquid", and "an aerosol" (*supra*) do not enjoy the necessary priority date. Second, the '441 makes no mention of intratracheal instillation devices (*i.e.*, for example, a bronchoscope) or a nebulizer.

In conclusion, neither the '441 patent nor the '059 application meet the legal standards to support a *prima facie* case of obviousness. Applicants, therefore, respectfully request the Examiner to withdraw the rejection.

IX. CONCLUSION

Appellants submit that, with due consideration to all these factors discussed above, the patentability of claims 22-25 and 27-37 is evident. First, the only reference cited by the Examiner (Gosselin *et al.*) is not prior art for several claim elements (*i.e.*, "a sterile solution" and "an aerosol". Second, the Examiner has improperly ignored claim elements that confer patentability. Third, even if the standards regarding a *prima facie* case of obviousness are applied against Gosselin *et al.*, the rejection fails.

For the foregoing reasons, it is submitted that the examiner's rejections of Claims 22-25 and 27-37 were erroneous, and reversal of these rejections is respectfully requested.

Respectfully submitted,
MEDLEN & CARROLL, LLP

Dated: Jan 3, 2004

By: _____
Peter G. Carroll
Reg. No.: 32,837

Attorneys for Appellant

X. APPENDIX A: CLAIMS INVOLVED IN THE APPEAL

22. A solution for the treatment of a microbial infection, said solution comprising a sterile liquid vehicle, an antibiotic and a leukotriene dissolved in said sterile liquid vehicle, wherein said solution is an aerosol.

23. The solution of Claim 22, wherein said leukotriene is leukotriene B_4.

24. The solution of Claim 22, wherein said leukotriene is a cysteinyl leukotriene.

25. The solution of Claim 24, wherein said cysteinyl leukotriene is selected from the group consisting of leukotriene C_4, leukotriene D_4, and leukotriene E_4.

27. The solution of Claim 22, wherein said microbial infection comprises *Klebsiella pneumoniae* infection.

28. A solution for the treatment of a microbial infection, said solution comprising a sterile liquid vehicle, an antibiotic and a leukotriene dissolved in said sterile liquid vehicle, wherein said solution is in an intratracheal instillation device, said instillation device is selected from the group consisting of an endotracheal tube and a bronchoscope.

29. The solution of Claim 28, wherein said leukotriene is leukotriene B_4.

30. The solution of Claim 28, wherein said leukotriene is a cysteinyl leukotriene.

31. The solution of Claim 28, wherein said cysteinyl leukotriene is selected from the group consisting of leukotriene C_4, leukotriene D_4, and leukotriene E_4.

32. The solution of Claim 28, wherein said microbial infection comprises *Klebsiella pneumoniae* infection.

33. A composition for the treatment of a microbial infection comprising, a sterile liquid vehicle, an antibiotic and a leukotriene dissolved in said sterile liquid vehicle, wherein said solution is contained within a nebulizer.

34. The composition of Claim 33, wherein said leukotriene is leukotriene B_4.

35. The composition of Claim 33, wherein said leukotriene is cysteinyl leukotriene.

36. The composition of Claim 33, wherein said cysteinyl leukotriene is selected from the group consisting of leukotriene C_4, leukotriene D_4 and leukotriene E_4.

37. The composition of Claim 33, wherein said microbial infection comprises *Klebsiella pneumoniae* infection.